fubara/09975350

(FILE 'HOME' ENTERED AT 16:12:42 ON 01 AUG 2002)

FILE 'REGISTRY' ENTERED AT 16:12:50 ON 01 AUG 2002

L1 1 S MODAFINIL/CN

FILE 'CAPLUS, BIOSIS, USPATFULL, MEDLINE, USPAT2' ENTERED AT 16:15:45 ON 01 AUG 2002

L2 561 S L1

L3 1563408 S PARTICLE OR PARTICLES

L4 8 S L2 AND L3

L5 7 DUP REM L4 (1 DUPLICATE REMOVED)

fubara/09975350

=> d ibib abs kwic l5 1-7

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:293436 CAPLUS
DOCUMENT NUMBER: 136:315011
TITLE: Compositions comprising modafinil compounds
INVENTOR(S): Jacobs, Martin J.; McIntyre, Bradley T.; Patel, Piyush R.
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030414	A1	20020418	WO 2001-US31904	20011011
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002098240	A1	20020725	US 2001-975350	20011011

PRIORITY APPLN. INFO.: US 2000-640824 A 20000817
US 2000-239490P P 20001011

AB **Particle**-forming compns. of modafinil compds., and aq. compns. of **particles**, wherein the **particles** comprise a modafinil compd., are disclosed, along with methods of their prepn., and their use in the treatment of diseases. A compn. was prepd. contg 90% PEG 400, 5% Span20, and 5% Capmul MCM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB **Particle**-forming compns. of modafinil compds., and aq. compns. of **particles**, wherein the **particles** comprise a modafinil compd., are disclosed, along with methods of their prepn., and their use in the treatment of diseases. A compn. was prepd. contg 90% PEG 400, 5% Span20, and 5% Capmul MCM.

IT **68693-11-8**, Modafinil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising modafinil compds.)

L5 ANSWER 2 OF 7 USPATFULL
ACCESSION NUMBER: 2002:157693 USPATFULL
TITLE: Compositions including modafinil for treatment of attention deficit hyperactivity disorder and multiple sclerosis fatigue
INVENTOR(S): Miller, Matthew S., Newtown, PA, UNITED STATES
Scammell, Thomas E., Wellesley, MA, UNITED STATES

fubara/09975350

PATENT ASSIGNEE(S): Cephalon, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002082301	A1	20020627
APPLICATION INFO.:	US 2001-29306	A1	20011220 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-638353, filed on 15 Aug 2000, PATENTED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-149612P	19990816 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Cephalon, Inc., 145 Brandywine Parkway, West Chester, PA, 19380
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
LINE COUNT: 694
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Modafinil is effective in improving symptoms of attention deficit hyperactivity disorder and symptoms of multiple sclerosis fatigue. The administration of modafinil is also shown to activate the tuberomamillary neurons of the posterior hypothalamus, and thus exhibits activity in an area of the brain associated with normal wakefulness functions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of sleep apneas of central origin (U.S. Pat. No. 5,612,378). U.S. Pat. No. 5,618,845 describes modafinil preparations of a defined **particle** size less than about 200 microns that is more potent and safer than preparations containing a substantial proportion of larger **particles**.
IT **68693-11-8**, Modafinil
(modafinil for treatment of attention deficit hyperactivity disorder and multiple sclerosis fatigue)

L5 ANSWER 3 OF 7 USPATFULL
ACCESSION NUMBER: 2002:29402 USPATFULL
TITLE: Compositions including modafinil for treatment of attention deficit hyperactivity disorder and multiple sclerosis fatigue
INVENTOR(S): Miller, Matthew S., Newtown, PA, United States
Scammell, Thomas E., Wellesley, MA, United States
PATENT ASSIGNEE(S): Cephalon, Inc., West Chester, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6346548	B1	20020212
APPLICATION INFO.:	US 2000-638353		20000815 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-149612P	19990816 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED

fubara/09975350

PRIMARY EXAMINER: Cook, Rebecca
LEGAL REPRESENTATIVE: Hrubiec, Robert T., Voelk, Eric K.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 614
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Modafinil is effective in improving symptoms of attention deficit hyperactivity disorder and symptoms of multiple sclerosis fatigue. The administration of modafinil is also shown to activate the tuberomamillary neurons of the posterior hypothalamus, and thus exhibits activity in an area of the brain associated with normal wakefulness functions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of sleep apneas of central origin (U.S. Pat. No. 5,612,378). U.S. Pat. No. 5,618,845 describes modafinil preparations of a defined **particle** size less than about 200 microns that is more potent and safer than preparations containing a substantial proportion of larger **particles**.
IT **68693-11-8**, Modafinil
(modafinil for treatment of attention deficit hyperactivity disorder and multiple sclerosis fatigue)

L5 ANSWER 4 OF 7 USPATFULL
ACCESSION NUMBER: 2001:188739 USPATFULL
TITLE: Low dose modafinil for enhancement of cognitive function
INVENTOR(S): Miller, Matthew, Newtown, PA, United States
Contreras, Patricia C., San Diego, CA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001034373	A1	20011025
APPLICATION INFO.:	US 2001-779417	A1	20010208 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-181283P	20000209 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CEPHALON, INC., 145 BRANDYWINE PARKWAY, WEST CHESTER, PA, 19380-4245
NUMBER OF CLAIMS: 60
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 729
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Modafinil is shown to be effective in improving or restoring cognitive function in the humans or other mammals when administered at doses that are substantially lower than optimal wakefulness-promoting doses. Daily dosages of less than 100 mg/day and more particularly from about 1 to about 75 mg/day are shown to be effective.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . apneas and disorders of central origin (U.S. Pat. No. 5,612,378). U.S. Pat. No. 5,618,845 describes modafinil preparations of

a defined **particle** size less than about 200 microns that is more potent and safer than preparations containing a substantial proportion of larger **particles**.

IT **68693-11-8**, Modafinil
(low-dose modafinil delivery system for enhancement of cognitive function in humans)

L5 ANSWER 5 OF 7 USPATFULL

ACCESSION NUMBER:	1998:150371 USPATFULL
TITLE:	Extrusion and freeze-drying method for preparing **particles** containing an active ingredient
INVENTOR(S):	Nguyen, Thanh-Tam, Limeil-Brevannes, France Jacquot-Leyder, Joelle, Creteil, France
PATENT ASSIGNEE(S):	Laboratoire L. Lafon, Maisons Alfort Cedex, France (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5843347		19981201
APPLICATION INFO.:	US 1997-906004		19970804 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-530293, filed on 19 Sep 1995, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1993-3316	19930323

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Silbaugh, Jan H.
ASSISTANT EXAMINER:	Jones, Kenneth M.
LEGAL REPRESENTATIVE:	Hoffmann & Baron, LLP
NUMBER OF CLAIMS:	15
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	910

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a process for the preparation of **particles** each comprising an excipient forming a matrix and at least one active ingredient uniformly distributed in the mass of said matrix, said process, which comprises the operations of extrusion and then lyophilization, being characterized in that it comprises the steps consisting of

(1.) the preparation of a homogeneous mixture from

(a) at least one active ingredient,

(b) a physiologically acceptable hydrophilic excipient, and

(c) water

to give a pasty mixture with a viscosity below 1 Pa.s, measured at room temperature (15.degree.-20.degree. C.);

(2.) the extrusion of the resulting homogeneous mixture and the cutting of the extrudate to give moist **particles**;

(3.) the freezing of the resulting **particles** as they fall

under gravity through a stream of inert gas at a temperature below 0.degree. C.; and

(4.) the freeze drying of said **particles**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Extrusion and freeze-drying method for preparing **particles** containing an active ingredient

AB The present invention relates to a process for the preparation of **particles** each comprising an excipient forming a matrix and at least one active ingredient uniformly distributed in the mass of said. . .

AB (2.) the extrusion of the resulting homogeneous mixture and the cutting of the extrudate to give moist **particles**;

AB (3.) the freezing of the resulting **particles** as they fall under gravity through a stream of inert gas at a temperature below 0.degree. C.; and

AB (4.) the freeze drying of said **particles**.

SUMM The present invention relates to a novel process for the preparation of isolated **particles**, each of which contains at least one active ingredient useful in therapeutics, cosmetics, dietetics or nutrition, by extrusion and then. . .

SUMM It further relates, by way of novel industrial products, to said **particles** consisting of an intimate association of a physiologically acceptable excipient and at least one active ingredient and obtained by said. . .

SUMM These **particles**, which are hereafter called "microparticles" and have a maximum size of between 0.05 mm and 5 mm, are obtained substantially. . .

SUMM . . . die, especially by means of a blade or by means of periodic vibrations, and (iii) the drying of the resulting **particles**, which generally fall under gravity, by means of an ascending inert gas (i.e. an inert gas circulating in countercurrent to the path of the **particles**). In this connection, see on the one hand published European patent application EP-A-0 204 596, which describes the preparation of. . .

SUMM the chemical stability, which avoids degradation of the molecules present in the form of fine active **particles**, and

SUMM Finally, lyophilization contributes to the surface treatment of the **particles**, increasing their hydrophilic character. Thus, in water, oral lyophilizates based on active ingredients which are normally insoluble or sparingly soluble. . . as a result of treatments such as micronization, dispersion, surface treatments, etc. Furthermore, the porous structure of lyophilizates prevents the **particles** from agglomerating when said lyophilizates are dispersed in water: the integrity of the original **particle** size is respected and particularly troublesome electrostatic phenomena are eliminated.

SUMM There is also a need to provide matrix **particles** of the abovementioned type which have the advantages of lyophilizates.

SUMM . . . it is proposed to provide a novel technical solution, involving extrusion and lyophilization, for meeting the above-mentioned needs and obtaining **particles** of regular geometric shape which have the advantages conferred by lyophilization. This novel technical solution, which comprises extruding a pasty. . . and (ii) to consequently use a

fusible lipidic material in which the active ingredient was solubilized in order to obtain **particles** of regular geometric shape after solidification.

SUMM . . . first feature of the invention, it is proposed to provide a process for the preparation of isolated and geometrically regular **particles**, each of the type consisting of a matrix of excipient containing at least one active ingredient in its mass, said process avoiding the agglomeration of said **particles** with one another or with the walls of their receptacle during their formation.

SUMM According to a second feature of the invention, it is proposed to provide **particles** obtained by this process, namely by the extrusion of a pasty mixture containing water, followed by lyophilization, said **particles** each containing at least one therapeutically, cosmetically, dietetically or nutritionally active ingredient which is useful in both man and animals.

SUMM . . . to a third feature of the invention, it is proposed to provide a conditioning process in which each of said **particles** is covered with a continuous-wall polymer coating. As will be seen below, the coating technique used according to the invention. . .

SUMM The object of the invention is achieved by a novel technical solution for the preparation of matrix **particles** by extrusion or forming and then lyophilization.

SUMM According to the invention, a process is recommended for the preparation of **particles** useful especially in therapeutics, each **particle** comprising an excipient forming a matrix and at least one active ingredient uniformly distributed in the mass of the matrix,. . .

SUMM the extrusion of said pasty mixture and the cutting of the resulting extrudate into moist **particles** with a size generally of between 0.01 and 5 mm,

SUMM the freezing of said **particles** by contact with an inert fluid at a temperature below 0.degree. C., and then

SUMM the drying of said frozen **particles** by freeze drying.

SUMM The freezing is effected as the moist **particles** fall through a cooled gaseous fluid, preferably circulating in countercurrent.

SUMM The **particles**, optionally coated with a continuous-wall polymer membrane, which have been obtained by said process and have a maximum size of. . .

DRWD FIG. 3 schematically represents a **particle** according to the invention (in this case a microbead) obtained by extrusion, lyophilization and then coating.

DETD The process according to the invention makes it possible to obtain **particles** (called "microparticles" here) of regular geometric shape which is of the type consisting of a matrix of excipient containing at. . .

DETD The process according to the invention for the preparation of **particles** each comprising an excipient forming a matrix and at least one active ingredient uniformly distributed in the mass of said. . .

DETD (2.) the extrusion of the resulting homogeneous mixture and the cutting of the extrudate to give moist **particles**;

DETD (3.) the freezing of the resulting **particles** as they fall under gravity through a stream of inert gas at a temperature below 0.degree. C.; and

DETD (4.) the drying of said **particles** by freeze drying.

DETD (5.) the coating of each of the lyophilized **particles** (i.e. the **particles** dried by freeze drying) with a continuous-wall

polymer membrane.

DETD . . . be liquid or pulverulent and it can also be either soluble or insoluble in water. When it is pulverulent, its **particle** size will be between 1 and 1000 .mu.m. As an excessive **particle** size (for example greater than or equal to 500 .mu.m) does not make it possible to obtain the smallest sizes. . . the invention when said active ingredient is insoluble in water, it is recommended to use active ingredient powders with a **particle** size of between 1 and 200 .mu.m. Powders with a **particle** size of 1-30 .mu.m are obtained by air-jet micronization and a **particle** size of 30-200 .mu.m is obtained by grinding. When the pulverulent active ingredient is insoluble in water, it will be. . .

DETD The lactose, polysorbate 60 and dextran 70,000 are dissolved in the water, the paracetamol (of **particle** size 50-200 .mu.m) is added and the ingredients are dispersed by means of a homogenizer operating at an angular velocity. . .

DETD The resulting lyophilized microbeads have an excellent mechanical strength and a **particle** size of 1.200 mm.

DETD is used to prepare microbeads according to the modalities described in Example 1, the differences being that the **particle** size of the probucol is 2 to 10 .mu.m and the dies have a diameter of 0.6 mm. This gives. . .

DETD is used to prepare microbeads according to the operating modalities described in Example 1, the differences being that the **particle** size of the piroxicam is 2 to 5 .mu.m and the dies each have a diameter of 0.2 mm. This. . .

DETD . . . the extruder and then the reproduction of the operating modalities described in Example 2. The lyophilized microbeads obtained have a **particle** size of 1.5 mm.

DETD . . . g

Hydroxypropyl .beta.-cyclodextrin	100 g	--
Lactose or mannitol	--	40 g
Xanthan gum	1 g	1 g
Water	200 g	200 g

Note

***particle** size of the modafinil: 2-5 .mu.m are used to prepare microbeads according to the invention.

DETD . . . acid 5 g 5 g

Aspartame	6	g	6	g
Mannitol	50	g	--	
Beta-cyclodextrin	--	50	g	
Water	300	g	300	g

Note

***particle** size of the dexfenfluramine: 5-10 .mu.m are used to prepare microbeads according to the invention.

CLM What is claimed is:

1. A process for the preparation of **particles** each comprising an excipient forming a matrix and at least one active ingredient uniformly distributed in the mass of said. . . C. (2.) extruding the resulting homogeneous mixture at a temperature above 0.degree. C. and

fragmenting the extrudate to give moist **particles**; (3.) freezing the moist **particles** as they fall under gravity through a countercurrent stream consisting essentially of inert gas at a temperature below 0.degree. C. to give at least partially frozen **particles**; and (4.) drying said at least partially frozen **particles** by freeze drying.

. . . (3.) comprises initiating said freezing by circulating said stream of inert gas in countercurrent to the path of the moist **particles**, and then continuing said freezing down to a temperature in the range -18.degree. to -80.degree. C. in a lyophilizer.

. . . process according to claim 1 further comprising, after step (4.), the step of (5.) coating each of the resulting lyophilized **particles** with a continuous-wall polymer membrane.

IT 50-99-7, Glucose, biological studies 56-40-6, Glycocol, biological studies 57-50-1, Saccharose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 79-10-7D, Acrylic acid, polymers 79-41-4D, Methacrylic acid, polymers 103-90-2, Paracetamol 108-73-6, Phloroglucinol 846-49-1, Lorazepam 3239-44-9, Dexfenfluramine 3505-38-2, Carbinoxamine maleate 6964-20-1, Tiadenol 7585-39-9, .beta.-Cyclodextrin 7585-39-9D, .beta.-Cyclodextrin, hydroxypropyl ethers 7631-86-9, Silica, biological studies 9000-01-5, Gum arabic 9000-65-1, Tragacanth Gum 9000-69-5, Pectins 9003-39-8, Pvp 9004-32-4, Cmc 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, ethers 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9005-32-7D, Alginic acid, derivs. 9012-76-4, Chitosan 9050-36-6, Maltodextrin 11138-66-2, Xanthan 12619-70-4, Cyclodextrin 23288-49-5, Probucol 25086-15-1, Eudragit l 100 25322-68-3, Peg 36322-90-4, Piroxicam 51166-71-3, Dimethyl .beta.-cyclodextrin 52519-63-8D, Carboxymethylchitin, ethers 53179-11-6, Loperamide **68693-11-8**, Modafinil 82101-10-8, Flerobuterol
(extrusion and freeze-drying method for prepg. pharmaceutical particles)

L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 1997:262706 CAPLUS
DOCUMENT NUMBER: 126:308803
TITLE: Acetamide derivative having defined **particle** size
INVENTOR(S): Grebow, Peter E.; Corvari, Vincent; Stong, David
PATENT ASSIGNEE(S): Cephalon, Inc., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5618845	A	19970408	US 1994-319124	19941006
GB 2293103	A1	19960320	GB 1995-24328	19951004
GB 2293103	B2	19970507		

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CA 2201967 AA 19960418 CA 1995-2201967 19951004
WO 9611001 A1 19960418 WO 1995-US12944 19951004
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9539514 A1 19960502 AU 1995-39514 19951004
AU 703087 B2 19990318
EP 731698 A1 19960918 EP 1995-937389 19951004
EP 731698 B1 20000112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 09511754 T2 19971125 JP 1995-512675 19951004
JP 2915146 B2 19990705
BR 9509257 A 19980707 BR 1995-9257 19951004
HU 77778 A2 19980828 HU 1998-737 19951004
EP 966962 A1 19991229 EP 1999-202603 19951004
EP 966962 B1 20010221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
AT 188607 E 20000115 AT 1995-937389 19951004
ES 2142499 T3 20000416 ES 1995-937389 19951004
AT 199216 E 20010315 AT 1999-202603 19951004
EP 1088549 A1 20010404 EP 2000-125091 19951004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
ES 2156457 T3 20010616 ES 1999-202603 19951004
RU 2171674 C2 20010810 RU 1997-108161 19951004
PL 181523 B1 20010831 PL 1995-319480 19951004
LT 4303 B 19980325 LT 1997-60 19970403
FI 9701417 A 19970404 FI 1997-1417 19970404
NO 9701541 A 19970604 NO 1997-1541 19970404
LV 11852 B 19980320 LV 1997-55 19970404
AU 9935090 A1 19990819 AU 1999-35090 19990616
AU 729586 B2 20010208
PRIORITY APPLN. INFO.: US 1994-319124 A 19941006
AU 1995-39514 A3 19951004
EP 1995-937389 A3 19951004
EP 1999-202603 A3 19951004
WO 1995-US12944 W 19951004

AB Pharmaceutical compns. comprising modafinil (I) in the form of **particles** of defined size (95% of total **particle** having diam. .ltoreq.200 .mu.m) are claimed. The **particle** size of modafinil can have a significant effect on the potency and safety profile of the drug. I powder having mean **particle** size of 50.18 .mu.m has faster dissoln. rate than those having mean **particle** size of 94.05 .mu.m and had plasma conc. of 10 .mu.g/mL as compared with 8.mu.g/mL.

TI Acetamide derivative having defined **particle** size

AB Pharmaceutical compns. comprising modafinil (I) in the form of **particles** of defined size (95% of total **particle** having diam. .ltoreq.200 .mu.m) are claimed. The **particle** size of modafinil can have a significant effect on the potency and safety profile of the drug. I powder having mean **particle** size of 50.18 .mu.m has faster dissoln. rate than those having mean **particle** size of

94.05 .mu.m and had plasma conc. of 10 .mu.g/mL as compared with 8.mu.g/mL.

ST acetamide deriv **particle** size pharmaceutical; modafinil **particle** size pharmaceutical safety

IT Dissolution rate
Drug delivery systems
Particle size
(acetamide deriv. having defined **particle** size)

IT Sleep
(narcolepsy; acetamide deriv. having defined **particle** size)

IT **68693-11-8**, Modafinil
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(acetamide deriv. having defined **particle** size)

L5 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:686623 CAPLUS
DOCUMENT NUMBER: 121:286623
TITLE: Extrusion and freeze-drying method for preparing pharmaceutical **particles**
INVENTOR(S): Nguyen, Thanh-Tam; Jacquot-Leyder, Joelle
PATENT ASSIGNEE(S): Laboratoire L. Lafon, Fr.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421371	A1	19940929	WO 1994-FR281	19940315
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2702968	A1	19940930	FR 1993-3316	19930323
FR 2702968	B1	19950623		
CA 2156915	AA	19940929	CA 1994-2156915	19940315
EP 690747	A1	19960110	EP 1994-909968	19940315
EP 690747	B1	19970528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507940	T2	19960827	JP 1994-520710	19940315
AT 153562	E	19970615	AT 1994-909968	19940315
ES 2105663	T3	19971016	ES 1994-909968	19940315
US 5843347	A	19981201	US 1997-906004	19970804

PRIORITY APPLN. INFO.:
FR 1993-3316 19930323
WO 1994-FR281 19940315
US 1995-530293 19950919

AB A method for prepg. **particles** each of which consists of a carrier forming a matrix, and at least one active ingredient uniformly distributed throughout said matrix. The method comprises extrusion and freeze-drying steps, wherein (1) at least one active ingredient, a physiol. acceptable hydrophilic carrier, and water are uniformly mixed to give a pasty mixt. with a viscosity at room temp. (15-20.degree.) of under 1 Pa.s; (2) the resulting uniform mixt. is extruded and the extrudate is broken up into moist **particles**; (3) the resulting **particles** are frozen as they fall under their own wt. into an

inert gas stream at a below-zero temp.; and (4) said **particles** are freeze-dried. A mixt. of paracetamol 100.00, dextran 10.00, xanthan 0.05, lactose 15.000, polysorbate-60 0.40 and water 120.00 g was extruded to **particles** of 0.5 mm diam. which were then freeze-dried under N.

TI Extrusion and freeze-drying method for preparing pharmaceutical **particles**

AB A method for prepg. **particles** each of which consists of a carrier forming a matrix, and at least one active ingredient uniformly distributed throughout said matrix. The method comprises extrusion and freeze-drying steps, wherein (1) at least one active ingredient, a physiol. acceptable hydrophilic carrier, and water are uniformly mixed to give a pasty mixt. with a viscosity at room temp. (15-20.degree.) of under 1 Pa.s; (2) the resulting uniform mixt. is extruded and the extrudate is broken up into moist **particles**; (3) the resulting **particles** are frozen as they fall under their own wt. into an inert gas stream at a below-zero temp.; and (4) said **particles** are freeze-dried. A mixt. of paracetamol 100.00, dextran 10.00, xanthan 0.05, lactose 15.000, polysorbate-60 0.40 and water 120.00 g was extruded to **particles** of 0.5 mm diam. which were then freeze-dried under N.

IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(extrusion and freeze-drying method for prepg. pharmaceutical **particles**)

IT Pharmaceutical dosage forms
(freeze-dried, extrusion and freeze-drying method for prepg. pharmaceutical **particles**)

IT 50-99-7, Glucose, biological studies 56-40-6, Glycocol, biological studies 57-50-1, Saccharose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 79-10-7D, Acrylic acid, polymers 79-41-4D, Methacrylic acid, polymers 103-90-2, Paracetamol 108-73-6, Phloroglucinol 846-49-1, Lorazepam 3239-44-9, Dexfenfluramine 3505-38-2, Carbinoxamine maleate 6964-20-1, Tiadenol 7585-39-9, .beta.-Cyclodextrin 7585-39-9D, .beta.-Cyclodextrin, hydroxypropyl ethers 7631-86-9, Silica, biological studies 9000-01-5, Gum arabic 9000-65-1, Tragacanth Gum 9000-69-5, Pectins 9003-39-8, Pvp 9004-32-4, Cmc 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, ethers 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9005-32-7D, Alginic acid, derivs. 9012-76-4, Chitosan 9050-36-6, Maltodextrin 11138-66-2, Xanthan 12619-70-4, Cyclodextrin 23288-49-5, Probucol 25086-15-1, Eudragit l 100 25322-68-3, Peg 36322-90-4, Piroxicam 51166-71-3, Dimethyl .beta.-cyclodextrin 52519-63-8D, Carboxymethylchitin, ethers 53179-11-6, Loperamide **68693-11-8**, Modafinil 82101-10-8, Flerobuterol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(extrusion and freeze-drying method for prepg. pharmaceutical **particles**)